To assay a core antigen of virus, virus particles must be disrupted to expose or release the core antigen in order that the core antigen can be detected by a probe such as an antibody reactive with the core antigen. There are known methods to disrupt the viral particles to expose the core antigen. However, considering the case where the core antigen is detected by an assay agent comprising anti-core antigen antibody, if the sample originally contains antibodies against the core antigen, the antibodies interfere with the desired assay reaction. In fact, in many cases, virus-containing blood samples contain antibodies against the core antigen. Therefore, in addition to disruption of a viral particle so as to expose the core antigen, antibodies against the core antigen originally present in a sample must be inactivated prior to assay to carry out a highly sensitive assay.

On the other hand, if an agent for inactivating the antibodies is added, there is a possibility that the agent added to interact the antibodies may also inactivate an anti-core antigen antibody added as a probe for detection. Therefore, in the case where an agent for inactivating the antibodies originally present in a sample is added to a sample as a pretreatment, the added agent should be eliminated from the pretreated sample prior to assay. However, this involves a complicated process and requires a long time. Therefore, it is highly desirable to select a pretreatment condition which inactivates the antigens originally present in a sample, but does not affect an antibody added as a probe for the core antigen. The present invention provides such a desirable condition.

Namely, the present methods provide a pretreated virus-containing sample suitable for detection of the virus with a probe such as anti-viral antibody by, for example, an immunoassay, wherein

(1) the virus particle is disrupted (see the specification at page 6, line 26, page 16, lines 32 to 33, etc.);

(2) the virus antigen (specifically core antigen) is exposed or released (see page 6, line 27, page 16, lines 31 to 32, page 21, lines 31 to 32, page 16, line 36 to page 17, line 5, etc.);

(3) the antibodies against the virus antigen present in the sample are inactivated (see page 6, line 26, page 16, lines 32 to 33, page 19, lines 34 to 35, page 21, lines 32 to 33, etc.); and

(4) the pretreated sample can be readily subjected to immuno-assay without further treatment such as elimination of the added agent; (see page 17, lines 3 to 5) without affecting the assay (see page 21, lines 17 to 18).

To satisfy the above-mentioned conditions, the present invention uses at least (a) an anionic surfactant, and (b) an agent selected from the group consisting of an amphoteric surfactant, a nonionic surfactant and a protein denaturant.

More specifically, the anionic surfactant represented by SDS is used at a concentration of 0.5% or greater, and preferably 1% or greater (see Fig. 1); the amphoteric surfactant represent by CHAPS is used at a concentration of 0.1% or greater; the nonionic surfactant represented by Triton X100 is used at a concentration of 0.1% or greater and 0.75% or smaller; and the protein denaturant represented by urea is used at a concentration of 1M or more (see the English specification, page 22, lines 24 to 27).

2. The cited reference Cummins et al, USP No. 5,081,010, describes the same components as those of the present invention. However, as can be seen from column 4, lines 29 to 31, according to this reference, the anionic surfactant is used at a concentration of at least about 0.1%, and preferably from about 0.2 to about 1%. On the other hand, as can be seen from Fig. 1 of the present invention, a 1% or more concentration of SDS (representing anionic surfactant) is necessary for the preferred condition. The concentration of the anionic surfactant described in USP '010 cannot provide the above-mentioned advantages (effects) of the present invention.

According to USP '010, the concentration of nonionic surfactants is at least about 1%, and preferably from about 4 to about 10% (see, column 4, lines 14 to 17). On the other hand, as can be seen from Fig. 4 of the present invention, the concentration of

Triton X100 (representing nonionic surfactant) should be 0.75% or smaller. Again, the concentration of nonionic surfactant described in the USP '010 cannot provide the advantages (effects) of the present invention.

Therefore, not only new claims 32, 34 and 36, but also claims 31,33 and 35 are believed to be novel and inventive over the USP '010.

3. the cited reference Sharma et al, WO 92/19284 is directed to disinfection of blood products. The purpose of WO '284 is completely different from that of the present invention. This reference does not refer at all to the above-mentioned advantages (1) to (4) of the present invention. This reference does not refer to (2) exposure or release of the core antigen, (3) inactivation of anti-core antigen antibody originally present in the sample, and (4) readily use of the treated sample for core antigen assay without affecting the assay.

The Croyd et al reference, USP No. 6,074,646, refers to the use of the same surfactants for treatment of blood samples. In addition, Kokai 53-104724 describes the use of the same surfactants. However, as described above, the purpose of Sharma et al is completely different from that of the present invention, therefore, even if the compositions described in Kokai or Cloyd et al are applied to the method of Sharma et al, the present invention cannot be realized. In addition, there is no motivation at all to apply the Kokai or Cloyd et al compositions to the Sharma et al method. Therefore, a combination of the three references does not destroy the invention step of the present invention.

Applicants believe the present invention is allowable. However, if further clarification is required, applicants would appreciate receiving a telephone interview with the Examiner.

Respectfully submitted,

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